RSRB GUIDANCE ON RECRUITMENT AND INFORMED CONSENT

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Recruitment of Human Research Subjects

Recruitment of potential research subjects is considered the first step of the informed consent process. As such, each application submitted to the RSRB must include a recruitment plan. The plan should address how subjects will be identified, how the study team will approach potential subjects and how the recruitment material (if any) will be utilized. Alternately, if the study does not involve direct contact with subjects, a records review for example, the plan should address how subjects will be identified, whether the study team has routine access to data being reviewed and how the study team will obtain the data if they do not have routine access to it. The RSRB will review the plan to ensure that the selection of subjects is equitable, that it protects subject privacy and is free of coercion and undue influence.

“Coercion occurs when an overt threat of harm is intentionally presented by one person to another in order to obtain compliance. Undue influence, by contrast, occurs through an offer of an excessive, unwarranted, inappropriate or improper reward or other overture in order to obtain compliance.”

- The Belmont Report

Direct Advertising

All direct advertising for study subjects (i.e., advertising that is intended to be seen or heard by prospective subjects) must be submitted to the RSRB and approved prior to implementation.

- **Documents that should be submitted for review**: websites, web postings, newspaper, radio and TV advertisements, press releases (that provide contact information), posters, flyers and scripts (phone/oral) that are intended for prospective subjects.

- **Documents that do not need to be submitted for review**: communications intended to be seen or heard only by health professionals, such as “dear doctor” letters and doctor-to-doctor letters (even when soliciting for study subjects), news stories, and publicity intended for other audiences, such as financial page advertisements directed toward prospective investors.

The RSRB must review both the information contained in the advertisement, the mode of its communication as well as other visual effects, such as type size. This review is to confirm that the procedures for recruiting subjects are not coercive and that the recruitment material does not state or imply a certainty of favorable outcome or other benefits beyond what is outlined in the consent document and the protocol. This is especially important when a study may involve subjects who are likely to be vulnerable to undue influence, for example, financially constrained subjects.

Generally, advertisements should be limited to the information the prospective subjects need to determine their eligibility and interest. When appropriately worded, the following items may be included in advertisements:

- The name and address of the investigator and/or research facility (e.g., University of Rochester) and the person or office to contact for further information
- The purpose of the research (e.g., the condition under study or goal of the project)
- The general criteria, in summary form, that will be used to determine eligibility for the study (e.g., healthy adults between the ages of x and y)
- The time or other commitment required of the subjects
- A brief list of participation benefits, if any (e.g., a no-cost health assessment). Note: payments to subjects for participation are not benefits; they are given for incurred
expense for participation and as an incentive. Advertisements may state that subjects will be paid, but they should not emphasize the payment or the amount to be paid.

Consider the following additional points in drafting any advertisements:

- When advertisements are to be recorded for broadcast the principal investigator (PI) should request an RSRB review and approval of the wording of the advertisement (i.e., the script) prior to taping to avoid having to re-tape due to inappropriate wording. The final audio/video should also be submitted upon completion.
- Advertisements for investigational drug, biologic or device studies should not use terms such as “new treatment” or “new medication” without explaining that the test article is experimental. Nor should they claim, either explicitly or implicitly, that the test article is safe/effective or equivalent/superior to any other drug, biological, device or procedure. A phrase such as “you will receive new treatments” incorrectly implies that all study subjects will receive products of proven worth newly approved by the FDA.
- Advertisements should not promise “free medical treatment” when the intent is only to say subjects will not be charged for taking part in the investigation.

If an investigator decides that new or additional advertising for subjects are needed after the study has received RSRB approval or if revisions to the approved plan/materials are needed, an amendment must be submitted to the RSRB for review and approval prior to implementation.

**Advertising over the Internet**

According to the FDA, RSRB review and approval of listings of clinical trials on the internet provide no additional safeguard and is not required when the system format limits the information provided to basic information, such as: the title; purpose of the study; protocol summary; basic eligibility criteria; study site location(s); and how to contact the site for further information.

Examples of clinical trial listing services that do not require prospective RSRB approval include the National Institute’s of Health (NIH) ClinicalTrials.gov and ResearchMatch websites, the National Cancer Institute’s cancer clinical trial listing (Physician Data Query [PDQ]), the government-sponsored AIDS Clinical Trials Information Service (ACTIS) and the University of Rochester’s clinical trials listing. (Note: Although RSRB approval of the language provided in the listing service may not be required, as with all recruitment methods, if the listing is intended for recruitment purposes, the use should be indentified in the protocol/application as such.)

When the opportunity to add additional descriptive information is not precluded by the data base system, RSRB review and approval is required to assure that any additional information does not promise or imply a certainty of cure or other benefit beyond what is contained in the protocol and the informed consent document. Similarly, any other type of recruiting completed via websites, web postings or the use of social media should be submitted for RSRB review and approval.

**Access to Subjects**

Privacy and confidentiality protection is an additional concern that must be considered in developing a recruitment plan and therefore only investigators with routine access to their prospective subjects (or subject records) may recruit these individuals directly (“routine access” meaning the investigator already has a clinical/academic reason to know(review a subject’s record). While this is particularly important with studies that involve the use of protected health information (PHI), it is equally as important in social and behavioral research.

Examples of recruitment methods that would be permitted:

- A clinician approaches patients under his/her care about participation a study in which the clinician is part of the study team.
• A social worker who is not part of the study team approaches his/her clients about participation in a study and, if the client agrees, provides the study team the client’s contact information for follow up.
• A professor who is not part of the study team announces a new study that is being completed within department during one of his/her classes. Interested subjects are provided the study team’s contact information.
• A daycare director who is not part of the study team mails IRB approved letters to parents of children attending the daycare. Included in the letter is the study team’s contact information for parents to contact directly.

When principal investigators wish to recruit subjects from populations with which they do not have routine access (e.g., the patients of other physicians or students at a different school district) to a research study, they may not contact these potential subjects directly (i.e., no “cold calls”). The following procedure is to be used:

• The PI provides a written description of the project to the person having access and a relationship (e.g., the treating physician) with potential subjects, explaining that he/she would like to recruit subjects for research.
• The person with access makes the project description available so that potential subjects have the opportunity to consider whether or not they may wish to get more information about participation.
• Potential subjects can choose to contact the PI either by phone or in writing (e.g., returning a postcard provided in a mailing or calling the phone number provided on an advertisement) to gain further information and continue to consider the project.

Recruiting Subjects from Other Institutions

– When recruiting subjects from other institutions, IRB approval from that institution’s IRB is required. If the institution does not have an IRB, a letter of cooperation will need to be submitted. For example, if students will be recruited through a local school, documentation of the school district’s approval must be submitted to the RSRB prior to initiating any study activities at the school.

Recruiter/Receptionist Scripts & Screening Logs

The first contact prospective study subjects make is often with a recruiter/receptionist who follows a script to determine basic eligibility for the specific study. The investigator should assure the procedures adequately protect the rights and welfare of the prospective subjects. In some cases personal and sensitive information is gathered about the individual. The RSRB should have assurance that the information gathered during recruitment will be appropriately handled. A simple statement such as “confidentiality will be maintained” does not adequately inform the RSRB of the procedures that will be used to protect confidentiality. The acceptability of the procedures would depend on the sensitivity of the data gathered, including personal, medical and financial information.

Examples of issues for RSRB review: What happens to personal information if the caller ends the interview, declines participation, is found to be ineligible or simply hangs up? Are names of non-eligible subjects maintained in case they would qualify for another study? Are paper copies of records shredded? If an outside recruitment company is being utilized, will the information gathered be used for other purposes or sold to others?

Similarly, these same issues must be taken into consideration when screening logs will be utilized. Generally, this information should be collected in a de-identified format (e.g., noting that potential subject 1 declined due to the time commitment to participate or that subject 2 was not eligible because their body mass index was too high). If the information being collected on the screening log is identifiable (e.g., a name or a date of service will be collected), additional
protections must be put in place. A limited data set and data use agreement or waiver of HIPAA authorization for these subjects may need to be included with the RSRB application.

**Recruitment and Future Contact Databases**

Under University policy, databases established solely for research purposes require RSRB review and approval. Therefore separate approval for the creation of any recruitment or future contact databases may be required.

- **Required**: Subject contact information will be collected and pooled with other study subjects participating in other studies for future contact. The database may include subjects who have participated in previous/current research studies as well as individuals who have not yet participated in research but would like to in the future. (For example, multiple studies enrolling subjects with a specific disease are provided future contact options in each individual study’s consent form. All subjects that provide permission are entered into one common database.)

- **Not required**: Subject contact information will be collected for use in a single study or sub-study within the same RSRB application. (For example, subjects enrolling in one study are provided future contact options at the end of the study’s consent form for the purposes of long term follow-up and potential enrollment in related sub-studies. All subjects that provide permission are entered into one database specific to that one study.)

Protocols for any recruitment/future contact should address how the database will be used, what information will be maintained in the database, who controls the database and who has access to the database. Please contact your RSRB specialist for more information.

Any study that will use a recruitment/future contact database for the purposes of identifying potential subjects will need to describe the database in their submission and provide an explanation of how the database will be used. Depending on the nature of the database, you may need to verify that an investigator has access (is listed as study personnel) on the database (e.g., with department or disease specific databases approved within the institution). Other databases such as SONA or Mechanical Turk where users register and choose what studies to participate in don’t necessarily require such access permission but still need to be identified as a recruitment tool in the submission. Please contact your RSRB specialist for more information.

**RSRB Watermarked Recruitment Documents**

Upon approval, the RSRB expects that only RSRB watermarked recruitment documents will be used. Only the most recently approved version of the recruitment document should be used and, when applicable, they must be printed on department letterhead. Exceptions to this may be permissible under certain circumstances (for example, if a form letter has been approved and it is not possible to enter personalized names/addresses on the watermarked version). Please contact your RSRB specialist if these circumstances arise.

**Informed Consent**

Informed consent is a basic ethical obligation for researchers and is required by federal regulation. Informed consent is not a form. It is a process of information exchange that takes place between the prospective/enrolled subject and the investigator, before, during and sometimes after the research intervention or interaction. Thus, the informed consent process is not a single event, but continues as the study progresses. Subjects should feel free to ask questions at any time. The amount of information that needs to be presented both in writing (i.e.,
the consent document and related materials) and orally is directly related to the risk that the study presents and the complexity of the research procedures.

The manner and context in which information is conveyed is as important as the information itself. There must be no coercion or undue influence. Subjects must have sufficient time to decide and should be allowed to consult with family and/or others if needed.

The purpose of a consent form is to provide a written source of information and a place to document that a subject’s consent has been given before the start of the study. **Consent forms must be signed and dated by the subject (or the subject’s authorized representative) before any research procedures may begin.** The form is important because it serves as a baseline of information for initial presentation, a reference source during the study, and documentation of voluntary participation. The complete original signed consent form is retained in the investigator’s study records and a copy is given to the subject. Copies may be placed in the subject’s records (e.g., medical chart or school records) if appropriate.

The study plan/protocol needs to outline the consent process. It should describe who will obtain consent and how the process of informed consent will promote thoughtful decision-making by subjects. Steps taken to determine comprehension and to minimize undue influence should be explained, especially when the study will include vulnerable populations such as children and the terminally ill. If any (or all) subjects will not be capable of providing consent, the study plan/protocol needs to describe the process used to obtain permission of authorized representatives. If an auditor-witness and/or translator are to be used, the protocol should explain their function, identify when they are required as well as who qualifies to act as an auditor/witness/translator. Note that the use of family members as translators is generally not appropriate because of ethical concerns about the accurate relay of information. The protocol should also explain how consent will be documented and how the forms will be stored.

Subjects are considered to be “enrolled” in a study once they have given consent. In studies where a screening/selection process is needed, it may be necessary to obtain a separate consent for the screening in addition to the study consent. In either case, the process should be clearly described in the protocol.

**NOTE:** Only RSRB-approved investigators, co-investigators and sub-investigators may obtain consent. Everyone obtaining consent at UR must be trained through the HSPP/EPRP program and listed on the RSRB application.

**Elements of Consent**

Although each research study involving human subjects is unique, the federal regulations and the RSRB require that all consent forms contain the following information elements:

- An introduction, including a statement that the study involves research
- An explanation of the purpose(s) of the research
- Description of study procedures (identifying both standard of care procedures and any that are experimental)
- Expected duration of subject involvement
- A description of any reasonably foreseeable risks or discomforts of participation
- Benefits of participation to the subject or others
- Appropriate alternatives or course of treatment that might be advantageous to the subject (not applicable if the only alternative is non-participation)
- UR standard wording for compensation for injury (for studies involving greater than minimal risk)
- Confidentiality of Records statement (and, if applicable, HIPAA authorization)
• FDA-required statement that information about the trial has been, or will be, entered into a databank that is publicly accessible at http://www.ClinicalTrials.gov (for applicable trials only; to determine if this applies to your study see: http://prsinfo.clinicaltrials.gov/s801-fact-sheet.pdf). For questions or help with registration contact the CTSI’s Office of Regulatory Support.

• Contact persons (for questions about the research, research-related injury and subject rights)

• Statement that participation is voluntary

• Statement that subjects will receive a signed copy of the consent

Federal regulations and/or the RSRB require several other elements of information if they apply to the study and are important for subject to know. These additional elements most often apply to FDA-regulated studies. Additional elements include:

• A statement that the particular treatment or procedure may involve risks to the subject that are currently unforeseeable
  o Include for research involving investigational or marketed drugs or devices for which toxicities are not well-studied in humans (e.g., phase 1 studies).

• A statement that, if the participant is or becomes pregnant or father a child, the particular treatment or procedure might involve risks to the embryo or fetus, which are currently unforeseeable
  o Include for research involving investigational or marketed drugs or devices for which effects to a fetus are unknown.

• Anticipated circumstances under which the subject’s participation may be terminated by the investigator without regard to the subject’s wishes (e.g., side effects of a study drug are too severe or the sponsor terminates the study)

• Payments (incentives and/or expense reimbursements if any)

• Additional costs to participate (e.g., hospitalization, cost of testing or transportation to and from the research site)

• Consequences of withdrawal and procedures for withdrawal that protect the subject’s safety
  o Include if any adverse health or welfare effects may be anticipated (e.g., the need to taper a drug treatment), or whether additional tests may be needed to help ensure the safety of the subject after withdrawal.
  o Remember that the consequences of withdrawal are not intended to coerce the subject into continuing to take part.

• Statement that subjects will be informed of new findings that may relate to their willingness to take part (e.g., if findings of a data & safety monitoring board raise safety concerns or new toxicities develop)

• Number of subjects (if this poses a risk to privacy, for example, or to provide the subject the risk exposure/context in which the study takes place)

• Probability of random assignment to placebo or experimental arm (e.g., one in two, like flipping a coin; or, one in four like drawing numbers from a hat)

• Statement of the entity sponsoring the study

• Conflict of interest statement(s) if applicable (both investigator and University)

Consent Issues in Research Involving Minors

In all research involving human subjects, the agreement to participate is an essential protection of their rights and welfare. Children, by definition, cannot give legal consent (per New York State, children are those persons under the age of 18). Therefore, a combination of assent (agreement) of the child subject and permission of the parent or legal guardian is generally deemed an adequate substitute. If either the parent refuses permission or the child subject refuses assent, the child cannot be enrolled.
As part of the review process, the RSRB will determine whether adequate provisions are made for soliciting both the permission of each child’s parent or legal guardian and the assent of the child. In some cases, the RSRB may find that the permission of one parent is sufficient. While this is typically based on the risk level assigned to the study, other factors regarding the nature of the study may be considered. In cases where both parent signatures are required, per federal regulations, “both parents must give permission unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child” (45 CFR 46.408[b]). Note that the RSRB does not consider parents who are unavailable due to scheduling conflicts to be “not reasonably available”.

In determining whether children are capable of assenting, the RSRB will take into account the ages, maturity and psychological state of the children involved. The judgment may be made for all children involved in the research under a particular protocol, or for each child, as the RSRB deems appropriate. Information must be presented in a language and format that is understandable to the child. The child should have an understanding of the research procedures and it should be clear that their participation is voluntary. In long-term studies where subjects are enrolled as children, but who will turn 18 while they are actively participating in the study, provisions must be made for obtaining their consent as adults after their 18th birthdays.

**NOTE:** One of the main goals of assent in studies is to let children know that they are not required to take part in the research, even if their parents say it is okay.

An exception to the assent mechanism can be made if the RSRB determines that either of the following is true:

- The capability of some or all of the children is so limited that they cannot reasonably be consulted.
- The intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well being of the children and is available only in the context of the research (e.g., children with life-threatening illnesses who are entered into open-label treatment protocols).

In these cases, the permission of the parent is sufficient, but the understanding of the child subjects is still desirable. Assent in the sense of agreement is not sought from the child subject because if he/she does not agree, the parent’s wishes will prevail. It would be disingenuous to ask for agreement when negative responses will be ignored. The non-agreement of the child, especially in older children (e.g., 17) may be ethically troublesome. The University medical center offers a Clinical Ethics Consultation Service that may be helpful to subjects, families and staff.

It is important to note that the permission of caregivers and/or service providers is not sufficient to conduct research with children. Only parents and legal guardians have that authority and responsibility.

- For children who are in foster care or are wards of the state, permission must be obtained from an individual who is authorized under state/local law to consent on the child’s behalf. With these cases, it is important to ensure that permission is being sought from the appropriate individual(s) and that documentation of this authority be maintained with the signed permission form.
- School principals, teachers, clinic personnel, etc., do not have the authority to give blanket permission for their students/patients/clients to participate in research. In classroom research, it must be made clear that the research is not part of the regular educational program and that the student’s grades or standing will not be affected by not participating.
Signature requirements for the child-subject’s assent and the parents’ permission depend upon the nature of the research. In most cases, parent permission should be documented on a signed permission form that follows the guidelines for consent forms. For assent, the federal regulations do not specify any specific elements that should be included in a form, nor do they provide guidance on signatures. Typically, the RSRB requires the use of an assent form for adolescents to sign and an assent script for younger children to document presentation of the information and the subject’s oral agreement. Refer to the RSRB’s Assent Document Templates for suggested elements to include in these forms. Table 1 below summarizes the University’s permission and assent documentation requirements.

**Waiver of Parental Permission** – The University of Rochester requires the permission of parents for research that involves subjects under the age of 18. There are four exceptions to this general policy which may be requested by investigators:

1) No-risk or minimal-risk research with older adolescents (e.g., anonymous surveys in high school students)
2) Purely observational studies (no intervention) of public behavior (e.g., classroom activities)
3) Studies of existing data and
4) Research with subjects under the age of 18 in those circumstances where New York Law expressly gives children the right to seek certain types of medical treatment without parental consent.

Depending on the nature of the study, the RSRB may require that the study team identify a research subject advocate who is independent from the study and available for consultation with research subjects as needed throughout the course of the study.

**NOTE:** Except for studies involving existing data, waiver of parental permission must be reviewed and approved by the Senior Associate Dean for Clinical Research, as a condition for RSRB approval.

Table 1: Summary of RSRB Permission / Assent Guidelines

<table>
<thead>
<tr>
<th>Subject Age Range</th>
<th>Document Type(s)</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>7 and under</td>
<td>Parent Permission</td>
<td>No assent script or form required</td>
</tr>
</tbody>
</table>
| 8-12 years        | Parent Permission + Assent Script | - Age-appropriate  
- Oral  
- Permits subject to opt out if parent(s) opt in  
- Signature of subject not required (but should document subject’s name)  
- Documentation of person obtaining assent |
| 13-17 years       | Parent Permission + Assent Form | - Age-appropriate  
- Written  
- Permits subject to opt out if parent(s) opt in  
- Signature of subject and person obtaining assent required |
<table>
<thead>
<tr>
<th>18 years and older</th>
<th>Consent form</th>
<th>When a child reaches 18 while participating in a study, the appropriate consent process should be conducted for the now adult subject to consent to participate in the research for him/herself.</th>
</tr>
</thead>
</table>
| Under 18: RSRB Determines Assent Not Required | Parent Permission | • No assent script or form required  
• Understanding of the child subject is still desirable |
| Under 18: Waiver of Parental Permission | Assent Form | • No parent permission form required  
• Appointment of advocate may be required |

** Note that the ages ranges provided above for obtaining assent from a child are only guidelines. The ages, maturity and psychological state of the children involved should be taken into consideration when determining whether and how to obtain assent.

**Consent Issues in Adult Subjects with Decisional Impairment**

The University has developed a policy delineating the consent process for adult subjects with decisional incapacity. To review the complete policy, see Appendix 1 of the RSRB Investigator Guidance.

Under this policy, the RSRB may approve enrollment into research with permission given by an authorized representative for:

1) Research not involving greater than minimal risk  
2) Research involving greater than minimal risk, but presenting the prospect of direct benefit to the individual subjects or  
3) Research involving a minor increase over minimal risk, with no prospect of direct benefit to individual subjects, but may produce knowledge about the subjects’ disorder or condition. (Note: this category requires additional approval by the Senior Associate Dean for Clinical Research and notification to URMC risk management office).

**Telephone permission by an authorized representative** - While the FDA allows investigators to obtain permission by telephone from a legally authorized representative, such practice presents ethical difficulties. The FDA’s position is as follows:

“A verbal [oral] approval does not satisfy the 21 CFR 56.109(c) requirement for a signed consent document, as outlined in 21 CFR 50.27(a). However, it is acceptable to send the informed consent document to the legally authorized representative (LAR) by facsimile and conduct the consent interview by telephone when the LAR can read the consent as it is discussed. If the LAR agrees, he/she can sign the consent and return the signed document to the clinical investigator by facsimile.”

RSRB approval of this process of obtaining permission will be limited to a case-by-case basis. Investigators wishing to obtain permission by telephone must clearly justify its rationale in the protocol.

**Consent to Tissue Banking**

Biological specimens include: blood & blood products, saliva, cells or tissue from any part of the human body, bodily products such as hair, sweat, breast milk, urine, etc. Studies involving the collection of biological specimens from research subjects require written informed consent from each donor-subject. Consent may be provided either as stand-alone document for studies where
the sole purpose of the study is to bank the tissue for future research or it may be included in a consent document where the tissue bank is only part of a study with several other procedures (for example, an investigational drug study banking leftover blood from samples provided a several time points throughout the course of the study). If the later method is used, the consent document can be written in a manner that either A) presents the banking as an optional part of the study (e.g., providing checkboxes to indicate the subject’s permission/refusal); or B) advises subjects that the specimens will be banked as part of their participation (note that in this manner, enrollment will then be limited to only those agreeing to participate in both the primary study and the tissue bank).

The consent document describing the tissue banking should include:

- The purpose for storing the tissue, including the type of research that will be conducted with the specimens
- Where the specimen will be stored
- Who will have access to the specimens and the conditions (if any) under which they will be released to investigators outside the original study team
- How long the specimens will be stored and whether they will be destroyed at any time point
- Procedures for protecting the privacy of subjects and maintaining confidentiality. Keep the following descriptors in mind:
  - Identified Samples = samples stored with an identifier
  - Single Coded Samples = samples stored without any identifiers but a key between the identifiers and the code on the sample is kept
  - Double Coded Samples = samples stored without any identifiers but the code on the sample links to a coded key; a second key, maintained elsewhere, links the first code to the identifiers
  - Anonymised Samples = samples that are initially single or double coded but the key to the linking codes has been destroyed
  - Anonymous Samples = samples with which identifiers were never collected or labeled
- Whether or not subjects would be re-contacted (or given the option to be re-contacted) regarding the banked specimens
- Who subjects should contact in the event they decide to withdraw their specimens and what will be done with withdrawn specimens
- Whether the results of any future testing will be provided to subjects
- Any risks/benefits and costs to subjects for banking

**Consent to Genetic Testing & Other Genetic Research**

Genetic testing presents additional risk beyond the risks related to obtaining a biological specimen and maintaining confidentiality. The results of a genetic test have the potential to drastically change an individual’s life and therefore additional protections must be considered.

*Section 79-L of the New York State Civil Rights Law* defines genetic testing and requires additional protections pertaining to genetic testing research. The regulation states that written consent must be obtained prior to performing a genetic test and has additional provisions for completing the tests. Studies that may not necessarily be doing genetic testing as defined by NYS law but may be doing other genetic research (e.g., gene expression) should also consider the following items in drafting their informed consent documents (and protocols).

- A general description of the test including a general description of the disease or condition being tested.
- The research purpose/use of the test and whether test results will be given to subjects.
- Referral for professional genetic counseling prior to signing the consent form.
• Whether/when samples will be destroyed or stored (if so, explain).
• A description of the procedures to protect data confidentiality.
• A statement of the right to withdraw consent to use of tissue for future use and how that can be initiated by the subject.
• A description of the special risks genetic testing may pose.

Waiver of Consent

The federal Common Rule regulations permit an alteration to some or all of the elements of informed consent or a complete waiver of consent for research subjects provided the following criteria are met (note that a waiver of consent is not permitted for FDA-regulated research):

1) The research is to be conducted by or under the approval of state or local government officials and is designed to study:
   • Public benefit or service programs;
   • Procedures for obtaining benefits or services under those programs;
   • Possible changes in or alternatives to those programs or procedures; or
   • Possible changes in methods or levels of payment for benefits or services under those programs;
     o And the research could not practicably be carried out without the waiver or alteration.
     o And the research is not subject to FDA regulation.

OR

2) The research meets all of the following criteria:
   • The research involves no more than minimal risk to the subjects
   • The waiver or alteration will not adversely affect the rights and welfare of the subjects
   • The research could not practicably be carried out without the waiver or alteration and
   • Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

Waiver of Consent for Deception Research – The RSRB recognizes that some otherwise ethically acceptable social/psychological research cannot be conducted with a complete description of its purpose; so some information must be temporarily withheld. Because subjects cannot truly consent without full information, the informed consent process is altered for approved studies involving deception. In applications and study plans, investigators using deception should address the following points:

• Consideration of the scientific value and validity of the research
• Consideration of the comparative efficacy of alternative procedures
• Assurances that deception would not influence subjects’ willingness to participate
• Provision of procedures for removing any harm through debriefing
• Assurances that the deception does not create inappropriate invasions of privacy
• Procedures for data handling when subjects decline to give consent to the use of their information

NOTE: Because deception research involves a waiver/alteration of consent, and the waiver/alteration may only be granted to studies involving minimal risk, deception studies may involve no greater than minimal risk.
Prior to data collection, subjects must have an opportunity to read and respond to information contained in a “Consent to Procedures.” This document should reveal as much as possible about the study and should include, at minimum, clear statements of:

- Study title
- Investigator names, department, and contacts
- What subjects will be asked to do
- Any risks associated with those activities
- Any payment or other reward for subject participation
- Unqualified opportunity to withdraw at any time without penalty
- Extension of the opportunity to ask questions and get answers
- Signature and date of the subject and person obtaining consent (unless the study qualifies for a waiver of documentation of consent).

Note that the “Consent to Procedures” itself should not be used as part of the deception and therefore should not include untruthful information. Any missing information should not put the subject at increased risk of harm or discomfort.

At the conclusion of participation, it is important that subjects be advised that deception has occurred, and be given the opportunity to withdraw or consent to have the data used. Subjects must have an opportunity to read and respond to additional information entitled, “Consent to Data Use” (see below), which will contain, at minimum, clear statements of:

- Study title
- Investigator names, department and contacts
- Full disclosure of the deception
- Unqualified opportunity to withdraw the data collected without penalty
- In addition, the following must be included:
  - A statement noting that a form of deception was used in the study.
  - A statement regarding data use, e.g., “I give my permission for the investigators to use the data I provided in this study. If I do not give my permission, I understand that the data I provided will be destroyed.”

Refer to the “Consent to Data Use” and Consent to Procedures” found on the RSRB web site and the sample language provided in Appendix 1 below for additional guidance.

**Waiver of Documentation of Consent**

The RSRB may also permit investigators to waive the requirement that the subject or the subject’s authorized representative sign a written consent form if it finds either:

- That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside the research context or,
- That the only record linking the subject and the research is the consent document and the principal risk is potential harm from breach of confidentiality (note that this waiver of documentation of consent is not permitted for FDA-regulated research).

When it considers waiving the requirement to obtain written documentation of the consent process, the RSRB may require the investigator to provide subjects with a written description of the study. Refer to the consent form templates for an example of such an “information sheet” to provide to subjects as well as Appendix 1 below for sample language.

**Consent through Oral Presentation and Short Form**
When investigators anticipate enrolling subjects who do not speak English, the RSRB requires that a translated version of the entire consent form and any other applicable study documents (e.g., surveys, drug compliance diaries or other study measures) be submitted for review and approval.

In the event that a non-English-speaking subject presents unexpectedly, the ethical requirement for complete information disclosure using a full translated consent form remains. Therefore, the default assumption is that the investigator will submit an amendment with the full translated document and obtain RSRB approval before enrolling the subject. The investigator must also determine if the lack of English proficiency will negatively affect the subject’s ability to participate in the study, i.e., understand and follow directions and be able to report problems.

In some special circumstances, usually because necessary clinical care/treatment is part of the research and the subject must be enrolled before a full translation can be developed and approved, the RSRB may approve the use of a “short form” consent document. If this occurs, complete the following:

- Submit an amendment request to the RSRB
- Include a short-form written consent document that states, in the subject's language (see the RSRB's Short Form Consent Template):
  - The title of the study
  - That the consent information for the research study was presented orally to the subject or the subject's authorized representative
  - The presentation included the purposes, risks, benefits and alternatives (if any) of participation
  - That participation is voluntary. The subject does not have to take part and can withdraw at any time
  - That the subject was given a copy of the full English version of the consent form and a copy of the short form
  - The name, signature line and date for the subject
  - The attestation, signature line and date for the witness (note that the witness must also sign the English consent form with the person obtaining consent)

Ensure that the following issues have been addressed:

- The short form consent states that the elements of disclosure required by regulations have been presented orally to the subject or the subject’s authorized representative. The full English version of the consent form embodies the basic and required additional elements of disclosure.
- There will be an adult witness to the oral presentation who is conversant in both English and the language of the subject (the witness must be unaffiliated with the research and it is best if the witness is a fluent professional). The translator should not be the same person as the witness.
- The subject or the subject’s authorized representative will sign and date the translated short-form consent document.
- The witness will sign both the translated short-form and the full English version.
- The person actually obtaining consent will sign a copy of the full English version.
- Copies of the translated short-form and the full English version will be given to the subject or the authorized representative.
- Both the original signed translated short-form and the signed full English version are to be kept in the research records with other signed consent forms.
- If the study team anticipates any additional non-English speaking subjects, a translated version of the entire consent document should be submitted for RSRB review.
Consent to Expanded Access or Single Patient Use

Sponsors and/or investigators may occasionally request RSRB review and approval of protocols using investigational drugs or devices (i.e., unapproved) in the clinical treatment of a patient(s). This mechanism provides seriously ill patients access to experimental drugs and devices when there are no satisfactory alternatives. Prospective RSRB approval review is required and clinicians must comply with the regulations pertaining to informed consent. Although this is still considered research under FDA regulations, consent wording for these activities differs from other research, in the following ways:

- The use of “patient” (vs. “subject”) and “doctor” or “treating physician” (vs. “investigator”) is permitted.
- “Research” is replaced with “treatment” or “treatment use.”
- The compensation for injury section is deleted (unless the sponsor makes provision for such compensation).
- The consent form must clearly indicate that the treatment use is experimental/investigational and has not yet been approved by the FDA.

Refer to the RSRB’s Consent Template “Consent Form for Treatment” for additional guidance.

Emergency Use of Unapproved Drugs and Medical Devices

Emergency use is defined as the use of an investigational drug, biological product or medical device (i.e., unapproved) with a human subject in a life-threatening situation in which no standard acceptable treatment is available [21 CFR 56.102(d)]. This does not include “off-label” uses of approved medical products in the practice of medicine (note, “off-label” use in a research context still requires RSRB review and approval). In these types of emergency-use situations, while a waiver of prior RSRB review may be permissible, waivers of other human subject protections, such as obtaining informed consent, may not apply.

Prior to initiating the procedure, the clinician/investigator must obtain informed consent of the patient or the patient’s authorized representative. In a medical emergency, it may not be possible to obtain informed consent. If both the clinician/investigator and a physician who is not otherwise participating in the emergency treatment certify all of the following in writing, prior consent may be waived on a case-by-case basis:

1) The subject is confronted by a life-threatening situation necessitating the use of the test article.
2) Informed consent cannot be obtained from the subject because of an inability to communicate with, or obtain legally effective consent from the subject.
3) Time is not sufficient to obtain consent from the subject’s authorized representative; and
4) There is no alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the subject’s life.

If immediate use of the test article is, in the clinician/investigator’s opinion, required to preserve the subject’s life, and if time is not sufficient to obtain an independent physician’s determination that the four conditions above apply, the clinician/investigator should make the determination and, within five working days after the use of the article, have the determination reviewed and evaluated in writing by a physician who is not participating in the clinical investigation.

The subject and/or the subject’s authorized representative must be notified of the use of the experimental procedure. Consent to continue should be obtained for emergency use/procedures requiring continued/repeat administration.
Drafting the Informed Consent Document

The informed consent documents are meant to act as the foundation of the information exchange between the study team and potential subjects. The document should provide potential subjects with enough information so that they can make an informed decision about whether to participate in the study and consent forms should be written in a manner that is clear and understandable to the study population.

Remember: The term “understandable” also pertains to the language commonly spoken by the subject population. Investigators who anticipate enrolling even one subject who only speaks a language other than English need to translate the entire consent form into that language. This translation may be done after an English form has been approved, but translated forms must be approved by the RSRB before use.

When drafting the consent form, the RSRB recommends working off the templates provided on the RSRB website. The templates provide instructions as well as standard language for several sections of the document. They should also be used in conjunction with the sample language provided in Appendix 1.

Keep the following additional points in mind:

- Information in the consent form must agree with the study plan/protocol and the RSRB application. It’s not uncommon for protocols to go through a number of revisions before and after they’re submitted to the RSRB. Some of these revisions may be to protocol elements that are explained in the consent form (e.g., the number/kind of tests). With each revision, make sure the protocol, application and consent are consistent (e.g., not 3 tests in the consent and 4 in the protocol).
- Aim for a 6th-8th grade reading level. Most word processors can generate reading level scores.
- Write as if you were talking to the subject (in 2nd person narrative, e.g., “you are being asked to…”) – in a conversational tone – not about the subject (in 3rd person objective, e.g., “he/she will be asked to…”). Use active rather than passive voice and keep pronoun usage consistent through the document. For example, rather than saying:
  - A pregnancy test will be administered to you/the subject will be given…
  - say:
  - You will have a pregnancy test.
- Do not use, “I understand that…” This terminology can be coercive, implying a level of understanding the subject may not have.
- Use the term “subject” instead of “participant” or “patient”.
- For clinical trials, use “study doctor” or “study investigator” instead of “principal investigator”.
- Use the term “payment” instead of “compensation”.
- The project title in the consent form may be the actual title on the review application and grant/contract, or, if it helps the subject understand the study, it may be simplified (as long as it isn’t incorrect or misleading).
- Replace scientific, medical and technical terms with lay terms. See Plain Language Resources in Appendix 3 for thesauruses and health literacy toolkits.
- Use subheadings and white space to improve readability in long forms.
• Use pictures, lists, bullets, tables and charts to help clarify complex schedules, study designs, and procedures. When using graphics ensure that they are
  o easy to understand,
  o have captions,
  o reproduce well,
  o are appropriately located and
  o are meaningful to the subject.
• List/Describe study procedures in a logical order (start at the beginning; end at the end).
• Use consistent terminology throughout the document. Spell out all abbreviations and acronyms when first used. Clearly define any scientific, medical or legal words.
• Use type-font no smaller than Times New Roman 12 point. Consent forms for elderly subjects and those with visual impairments may benefit from even larger type. Keep the font style and size consistent throughout the document.
• Try to keep words to 3 syllables or less. Keep sentences short, simple and direct. Keep paragraphs short, conveying one procedure/risk/etc. per paragraph/bullet.
• Consider providing a summary of highlights or supplemental “quick reference guide” with consent documents that are lengthy and potentially overwhelming.
• Include a footer that
  o numbers the pages (e.g., 1 of 6),
  o identifies the RSRB study number and
  o shows the version date . When entering the date in the footer, manually type in the date rather than selecting “Insert Date” from the footer toolbar; using “Insert Date” will automatically update the footer each time the document is opened resulting in incorrect version dates.
• When creating multiple consent documents for one study (e.g., an adult consent, authorized representative permission, parental permission and age-appropriate assents) consider combining the consent and permission documents. This can be accomplished by stating in the consent heading “If you are the parent of a child or the authorized representative of an adult subject who may be enrolled in this study, the use of the word ‘you’ in this form refers to the subject.”

Initial RSRB Review of Consent Documents

Once the consent document has been submitted with the RSRB application for initial approval, it will be reviewed by the RSRB specialist, chair and depending on the level of risk, the full board. The document will be reviewed to ensure that it will be understandable to the study population and that it is consistent with both the protocol and application. Any RSRB-required changes will either be described in writing or provided directly in a tracked document.

In reviewing tracked documents, be sure to review and accept each change and address any miscellaneous comments or questions noted directly in the document. Once you have made all of the necessary revisions and accepted the tracked changes, review the document for any additional grammatical or formatting errors. A clean, unmarked version of the document should then be uploaded into the application for confirmation review by the RSRB. Note that only a clean version of the revised consent document is required with new applications that have not yet been approved. Should you wish to provide a tracked copy of the document, please upload the tracked document with your response to the chair/board (in the ROSS system, once you click “Submit Changes to IRBS” a pop up box will appear; upload a copy of the tracked document here as opposed to section 83.1 of the application).

The Informed Consent Process

It is important to understand that informed consent is not just a signature on a form; it is a process of information exchange that takes place between the prospective/enrolled subject and the
investigator, before, during and sometimes after the experiment. The informed consent document itself is a description of what should have been communicated to potential subjects. The process not only includes reviewing and signing the informed consent document but may also include:

- Recruitment materials
- Oral instructions or explanations
- A question and answer period
- Assessing subject understanding
- Providing adequate time for the subject to review the form and consider their participation
- Providing new findings or study updates as appropriate throughout the study
- Periodic re-affirmation or re-consent as appropriate throughout the study

As part of the review process, the RSRB will evaluate the consent process outlined in the study protocol and application to ensure that the process is adequate given the nature of the study. In developing your consent process in your protocol, consider the following:

- Setting: Generally speaking consent discussions should occur in a private setting where your conversation won’t be overhead by others (this is particularly important when dealing with topics that are sensitive in nature). It’s also important to consider how the setting may affect your discussion. For example, if you are providing study information in a classroom setting there may be additional elements of peer pressure and inattentiveness to deal with.
- Timing: The consent process should be completed well in advance of any study intervention or procedure to give the subject sufficient opportunity to consider participation. It may take several meetings/discussions before the potential subject not only understands the study but, for clinical trials, the disease they may have just been diagnosed with and what their other treatment options may be.
- Minimizing Undue Influence: Vulnerable populations such as minors and students are particularly susceptible to influence from authority. Consider how you can remove the “intimidation factor” as appropriate. Healthcare providers have tremendous influence over patients within their clinical practice. Subjects may be too trusting of their healthcare providers and provide consent without a true understanding of what the study entails. Subjects may not want to antagonize healthcare providers by refusing to participate in a study. In these cases, it may be appropriate to consider delegating the consent responsibility to someone else on the study team.
- Use additional aids (videos, brochures, etc.) to explain study procedures and supplement the information provided in the consent document.
- Ask open-ended questions to potential subjects to assess their understanding of the study (e.g., “In your own words, tell me…what the study is about; what will happen to you if you decide to be in the study; what risks might you experience; what other options do you have.”)
- Discuss the study in the presence of “personal advisors” (friends/family members) who may aid in the subject’s decision making process.

**RSRB Expectations**

The University’s expectations, i.e., what you must do to comply with the approved consent process are outlined in the RSRB approval letters. Expectations concerning consent are the same regardless of the risk involved in the study. These letters state:

- Consent must be obtained and documented in the manner approved by the RSRB.
- Only consent forms bearing a current “RSRB Approved” watermark may be used.
- Only the most recently approved version of any consent or recruitment document may be used when obtaining consent.
• Principal Investigators are responsible for maintaining all approved pages of the signed consent forms for at least 3 years after the research is completed and closed in the RSRB files (6 years after the research is completed if HIPAA authorization is required), or for a longer term if required by FDA regulations or other contractual agreements.

• Consent forms/recruitment letters must be printed on department letterhead.

Practically speaking, what does this mean?

• How Consent is Obtained: The RSRB expects that you will obtain consent in the manner indicated in your application and protocol, and that, if you want to change the procedure, you will get the RSRB approval by means of an amendment request.

Here are some examples:

  o If the study eligibility criteria state that subjects must be able to consent for themselves, a relative or friend cannot sign the consent on behalf of the subject.
  o If the application and protocol indicate that only English-speaking subjects will be enrolled, consent cannot be obtained from an individual who doesn’t speak English.
  o If the study involves two different populations and two separate consent documents for each population – patients with illness and healthy controls, for example – the proper consent for each specific subject population must be used. This is particularly important when different subject populations undergo different study interventions or procedures.
  o If the protocol states that the Principal Investigator will obtain consent and no other personnel are listed, then only the Principal Investigator may sign consent documents as the person obtaining consent.

• How Consent is Documented (Signed): Here are some guidelines that will help ensure proper documentation of consent:

  o Unless documentation of the subject’s signature has been waived by the RSRB, make sure the consent form is signed and dated. Signatures are required from the subject (or subject’s representative) and routinely from the person obtaining consent (which is often, but not always, the investigator). Generally speaking, the person obtaining consent should sign the form on the same day as the subject. Signature dates separated by days may prompt auditors and the RSRB to question the consent process. If you anticipate that the signature dates of the subject and person obtaining consent will consistently be different – for example, if you’re obtaining written consent via mail after a telephone discussion – this should be described in the protocol.
  o Make sure the first page of the consent document is on department letterhead. It is recommended that consent/recruitment documents be submitted to the RSRB on electronic letterhead; however if this is not possible, the first page of the watermarked document should be printed on letterhead upon approval.
  o Make sure that any checkboxes on the form (e.g., indicating interest in additional testing or future studies) are completed.
  o Make sure that any witness signature blocks are completed. Generally speaking, it is expected that only individuals unaffiliated with the research will act as witnesses. If a witness is optional or required only in certain circumstances, this should be clarified in the protocol.
  o Remember that anyone obtaining consent must have completed the University’s research ethics training and must be approved by the RSRB (listed in sections 1.5-1.7 or 85.1 of the application). If any additional individuals will obtain consent, submit an amendment to the RSRB requesting that they be added to the study personnel – before they start obtaining consent.
- The RSRB expects that the original copy of the signed consent be maintained in the study file and that a complete copy of the consent form will be provided to the subject. Failure to keep these records may lead auditors/RSRB to question whether valid consent was obtained.
- To help ensure confidentiality, store the consent forms in a secure way (in a locked file cabinet, for example).
- DON'T sign or date the consent form for the subject (or the subject’s representative). Signed consent documents should be reviewed by the person obtaining consent prior to providing a copy to the subject to ensure that it is complete.
- DON'T use a signature stamp in place of an original signature for the person obtaining consent.
- DON'T white out, cross out or otherwise change any part of the RSRB-approved consent form. Any revisions to the consent form must be submitted as an amendment for RSRB review and approval.
  - It is acceptable for the person obtaining consent to use the back of forms/other white space to note questions the subject or family members asked, etc. as a way to document the consent conversation.
- Consider documenting the process for each subject in the progress note/case history. While federal guidelines do not specify that further documentation is required beyond that of signing/dating the consent form, FDA regulations specific to clinical trials conducted under an Investigational New Drug Application state that “the case history for each individual shall document that informed consent was obtained prior to participation in the study” (21CFR312.62[b]). Therefore, although contextual documentation of how and when the consent process occurs is not required for all studies, it is recommended as best practice. Documentation of any re-consent as described below should also be include in the study file.

- Using the Current RSRB-Watermarked Consent: The RSRB places a watermark on each page of every consent document it approves indicating the study number and expiration date. Points to consider:
  - The watermarked consent is the version the RSRB approved – and the only one the University recognizes as valid. To locate the watermarked documents:
    - Log into ROSS and click on the “Applications” tab;
    - Locate the study under the “Active” heading and click on the name of the study to continue;
    - On the horizontal toolbar at the bottom of the screen, click on the “Documents” tab;
    - Scroll down to locate your approved & watermarked consent and recruitment documents.
  - Make sure the date on the consent form is current. Review the document before presenting it to the potential subject. If the watermark indicates the study expired 1/15/12, for example, and the consent process is taking place on 3/20/12, valid consent won’t be obtained.
  - Remember that, each time the consent form is amended or the study is renewed, a new watermark is applied. In addition to the study approval expiration date, the new watermark will bear the date of the amendment’s or continuing review’s approval. It’s this version you’ll need to use. Keep one copy of the previous version in the study file, but throw out any unsigned copies to help ensure that only the current copies are available to the study staff and presented to potential subjects. If the consent forms are kept in more than one location, make sure all have been updated with the current version.
Ongoing Consent Issues after RSRB Approval

Storage of Informed Consent Documents

As noted above, Principal Investigators are responsible for maintaining all approved pages of the signed consent forms for at least 3 years after the research is completed and the RSRB file is closed (6 years if HIPAA authorization is required), or for a longer term if required by FDA regulations or other contractual agreements. In storing informed consent documents, keep the following points in mind:

- Signed consent documents are under the custody of your department. If the Principal Investigator leaves the institution, the original signed consents must remain at the University of Rochester.
- Designate one specific area to store all original copies of signed consent documents to decrease the chance of losing the documents.
- Store the signed documents in chronological order to aid in finding the last signed consent documents for continuing review.
- Consider maintaining a link between the consent document and subject number. In the event of an audit, it is important to be able to link signed consent documents to study data. Ideally study teams should keep an enrollment log separate from their database.
- Keep a blank copy of all approved consent documents in your study’s file.

Amending Consent Documents

Any changes to the consent form must have RSRB approval. These revisions may be as minor as an updated investigator telephone number or as major as the addition of a new experimental arm. Whatever the nature of the change, RSRB review and approval is required before the change may be implemented.

In submitting amended consent documents through the ROSS system, you will be asked to provide two versions of the revised consent documents: 1) a tracked version showing the proposed changes; and 2) a clean version with all the tracked changes accepted.

For instructions on completing the amendment within the ROSS system, click: http://www.rochester.edu/ohsp/rsrb/training/investigatorTraining.html

In amending consent documents, you will also need to consider whether current/past subjects will need to be informed of the change and potentially re-consented. Changes that are minor and do not affect subject participation (e.g., formatting, editorial or personnel changes) may not require notification and/or re-consent. A change to telephone numbers for contact may need to be relayed. Likewise, when more substantial changes are made (e.g., adding an additional procedure, changing subject payment, etc.) or when new information emerges that may affect their willingness to participate, these changes need to be communicated to subjects. Changes may be communicated orally or in writing via an information sheet/letter or a revised consent form depending on the nature of the change (note that any oral communications should be documented in the subject’s study file).

Ongoing RSRB Review of Consent Documents

At the time of continuing review, the RSRB requests a copy of the consent signed by the last subject enrolled. If the study has more than 1 approved consent document, a copy of the last signed form for EACH type of approved consent document should be submitted. The printed name and signature should be blanked out (on the copy submitted – not on the original) to protect subject privacy but do not obscure the subject’s written date of consent nor the name, signature
and date of the person obtaining consent. The RSRB reviews this document(s) to determine the following:

- Signatures and dates are appropriately provided.
- The person obtaining consent was approved by the RSRB.
- The entire, correct consent version was used.
- Each page contains the current RSRB watermark.
- The first page is on letterhead.

**Errors in Obtaining & Documenting Informed Consent**

Unfortunately, errors in obtaining and documenting informed consent are common and are typically either self-identified by the study team, found at the time of an audit or found when the RSRB reviews the last signed consent documents during continuing review. Common errors include:

- Using the incorrect form – an outdated version of the document or the wrong document for the study population (for example, using a written assent versus an oral script for a subject under the age of 12).
- Not printing the first page of the document on letterhead or not using a watermarked version of the document.
- Consent obtained by staff without HSPP/EPRP training and/or who have not been approved by the RSRB.
- Cross outs, additions or other revisions on the consent document.
- Initiating study procedures prior to obtaining consent.

Typically these errors are minor and may be remediated through a variety of actions depending on the circumstance. Regardless of the circumstance, the error must to be reported to the RSRB. Errors can be reported using 1 of 2 mechanisms: 1) Submit a Type 8 (Non-Compliance) Reportable Event using the RSRB Online Submission System; or 2) at the time of continuing review, report the error in question 5.8 of the progress report (Did any problems occur in the process of obtaining and documenting informed consent?). If you are unsure of which mechanism to use, consult with your RSRB specialist.

When errors are reported, the RSRB will review the event and determine if the remediation plan is appropriate. Corrective actions may include:

- Notification to the subject(s)
- Re-consent of the subject
- Documenting the error in a note to file
  - Notes to file are meant to provide additional information or clarification to study documents maintained in the study file and to explain any discrepancies or missing/incomplete data. To be valuable, the note to file should explain the discrepancy, the action taken to correct the discrepancy and the preventative action adopted to prevent similar discrepancies in the future.
- De-identification of the data
- Exclusion of the data

Note that although errors in obtaining and documenting informed consent are typically minor, if you fail to adhere to federal regulations and/or University policy regarding informed consent, you fail to obtain a legally effective informed consent. Failure to obtain legally effective informed consent may be considered serious non-compliance under federal regulations and repeated failures may be considered continuing non-compliance. Both serious non-compliance and continuing non-compliance must be reported to federal authorities. Please refer to the discussion
Re-Consent of Subjects

Throughout the course of a study, it may be necessary to re-consent subjects. Circumstances with which re-consent would be required include (but are not limited to):

- A minor that originally provides assent with parental permission and subsequently turns 18 during the course of study participation.
- A subject that was originally enrolled with the permission of an authorized representative regains capacity during the course of study participation.
- A subject given an unapproved drug/device without consent in an emergency regains the ability to consent.
- A subject that originally provides consent for their participation and subsequently loses capacity over the course of a study (permission from an authorized representative would then be required given that the protocol/application permit continued participation).
- The RSRB board or chair determines that re-consent is required after an incident of non-compliance has been reported.
- Substantial changes are made to the study (e.g., changes in risks or study procedures) or new information emerges regarding study participation.

In the event that a subject needs to be re-consented, ensure that only the most recently approved RSRB watermarked consent document is used and that the current date is used to document the date of re-consent (not the date prior consent was obtained).

Preventative Action Measures

Consider the following preventative action measures in creating and utilizing your consent documents throughout the course of a study:

- Incorporate electronic letterhead directly onto the 1st page of all consent documents submitted to the RSRB therefore eliminating the extra step of having to print them on letterhead.
- Identify only the Principal Investigator on the heading of the consent form. The more investigators listed in the heading, the more likely the need to revise the document with personnel changes. The more changes that are made to consent documents, the more likely it is that an outdated version of the document will be used inadvertently in obtaining consent.
- Do not include a space for subject initials on each page of the document or witness signature blocks unless necessary. OHRP and FDA only require a witness signature when a short form is used to document consent. For all other studies where witness signatures/subject initial lines are included in the consent document, it is best practice to address whether these items are mandatory or optional in the study protocol. If they are optional, the protocol should also address circumstances with which these fields should be completed.
- Develop a process for:
  - Maintaining copies of the current, approved, RSRB watermarked consent forms for use
  - Destroying outdated copies of consent forms
  - Ensuring that the signature page – including name, signature, date and any optional checkboxes – are completed at the time of consent
  - Providing subjects with a signed copy of the document
APPENDIX 1: Consent Document Sample Language

The purpose of this appendix is to provide sample language to be used in conjunction with the RSRB Consent Templates. Each item below provides sample language that may be used to describe study procedures and/or risks related to participation as appropriate. In some cases, additional sample language that has been further simplified for use in an assent documents is provided. Any sample language that is used while drafting a consent documents should be modified accordingly based on the study protocol. Please note the RSRB may require additional changes based on protocol and application review. Items are listed in alphabetical order and include:

<table>
<thead>
<tr>
<th>Allergic Reaction</th>
<th>HIV Testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Audio-Taping and/or Video-Taping</td>
<td>IV</td>
</tr>
<tr>
<td>Blinded Studies</td>
<td>Interview</td>
</tr>
<tr>
<td>Blood Draws</td>
<td>Invasion of Privacy/Breach in Confidentiality</td>
</tr>
<tr>
<td>Bone Marrow Aspiration / Biopsy</td>
<td>Lumbar Puncture</td>
</tr>
<tr>
<td>Bronchoscopy</td>
<td>MRI</td>
</tr>
<tr>
<td>Chart Review</td>
<td>Nasal Wash</td>
</tr>
<tr>
<td>Cognitive Testing</td>
<td>Oral Glucose Tolerance Test</td>
</tr>
<tr>
<td>Contrast Agent</td>
<td>PET Scan</td>
</tr>
<tr>
<td>CT Scan</td>
<td>Placebo</td>
</tr>
<tr>
<td>Discarded Tissue</td>
<td>Pregnancy</td>
</tr>
<tr>
<td>Discovery of Previously Unknown Condition(s)</td>
<td>Questionnaires</td>
</tr>
<tr>
<td>Dose Escalation</td>
<td>Radiation</td>
</tr>
<tr>
<td>DXA (Dexa Scan)</td>
<td>Randomization</td>
</tr>
<tr>
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Allergic Reaction

**Risks:** It is possible that you may have an allergic reaction to the study drug. This reaction may be mild, such as a skin rash, or you may have more severe symptoms like swelling of the throat, low blood pressure, and shortness of breath. In rare cases, a severe reaction could cause death.

Audio-Taping and/or Video-Recording

**Procedures:** Your interview will be audio-taped. Once the interview is complete, the tape will be used to make a transcription of your interview. Your name will not be included in the transcription. Once the transcription is complete the tape will be destroyed.

We would like to videotape one of your sessions. The videotape will be used to review and analyze your body language and interactions with the study team by the lead study site at the University of X. The videotape will be stored until the study has been completed and then it will be destroyed. Allowing us to videotape one of your training session is an optional part of this study. You will be asked to indicate your preference at the end of this form.

**Risks:** See “Invasion of Privacy/Breach in Confidentiality” below.

Prior to Signature Blocks: Please mark an X in the boxes below to indicate if you are willing to have one of your sessions taped.

- [ ] Yes, I agree to be taped.
- [ ] No, I do not want to be taped.

Blinded Studies

**Procedures:** Neither you nor the study team will know which treatment you are assigned. If there is an emergency, the study team will be able to find out quickly what group you were assigned to.

Blood Draws

**Procedures:** You will have a small blood draw about [1 teaspoon]) at [each study visit].

**Risks:** Blood draws may cause pain, redness, bruising or infection at the site of the needle stick. Rarely some people faint. The study team member may apply numbing cream to the area so that the needle stick won’t hurt as much.

Bone Marrow Aspiration / Biopsy

**Procedures:** You will be asked to have a bone biopsy and to donate bone marrow from your hip. Bone marrow is the soft material in the center of bones that produces new blood cells. The area will be numbed with lidocaine and, once numb, a large needle will be inserted through a small cut to draw about [4 tablespoons] of marrow out of the bone and to remove a small piece of bone. Your level of pain will be monitored throughout the procedure and you’ll be encouraged to voice any concerns. Additional numbing medicine may be utilized if necessary. The entire procedure will take about [1 hour] to complete. We will call you about 2 days after the procedure to see how you are doing.

**Risks:** The bone marrow aspiration and biopsy may cause pain, bruising, bleeding and infection. Soreness near the site may last for a couple of days after the procedure. You may have more pain, risk of bleeding and bruising if you complete both aspiration and biopsy rather than just the aspiration. If your pain is severe or you develop a fever, please contact the study team immediately.

Bronchoscopy

**Procedures:** If you decide to participate in this study, you will undergo a bronchoscopy. This procedure involves passing a long tube with a light on it through your nose and into your upper airway and lungs. Before the procedure begins, you will have a numbing spray applied to your
nose and throat and an IV (intravenous) needle with a tube attached put in the vein in your arm. Medication to make you drowsy and help you stay comfortable during the procedure will be given through the IV. The test will take [20-40 minutes] to complete. You'll be able to go home once you’re fully awake after the procedure, but should have someone drive you home.

**Risks:** The bronchoscopy is not typically painful but it may cause throat numbness, cough, a sore throat and fever. The numbing spray may make your mouth feel funny and has an unpleasant taste. Common side effects of the drug administered through the IV include feeling dizzy, faint, lightheaded, tired or out of breath. You will be watched closely throughout the procedure and we will treat any side effects that occur.

**Chart Review**

**Procedures:** As part of this study we will collect some information from your medical record. This will include information such as your age, sex, race, height and weight, pain level, number of blood transfusions, medications you are taking and the results of any laboratory or diagnostic tests.

**Risks:** See “Invasion of Privacy/Breach in Confidentiality” below.

**Cognitive Testing**

**Procedures:** You will undergo tests to assess your mood, memory, attention and mental functioning and to determine how clearly you are thinking. This will involve answering questions, performing paper and pencil tests and completing a test on the computer. This testing will take approximately [45 minutes] to complete.

**Risks:** You may experience feelings of frustration while taking the tests. These tests are meant to be challenging. You will be able to take breaks as necessary.

**Written Assent:** You will do some tests so we can find out how you pay attention to things and think. These tests will take about [45 minutes] to finish and might make you feel nervous or frustrated, or you might even get bored with them. You will be able to take breaks whenever you want to.

**Contrast Agent**

**Risks:** There is a chance of developing an allergic reaction from the contrast material, which may cause symptoms ranging from mild itching or a rash to severe difficulty breathing, shock or rarely, death. The contrast material may also cause kidney problems. The study doctors will do a blood test prior to the test to confirm that it is safe you to receive the contrast.

For IV contrast: You may feel discomfort when the contrast material is injected. You may feel warm, flushed, get a metallic taste in your mouth or, rarely, may make you vomit or feel sick to your stomach.

For oral contrast: You may experience vomiting, nausea, cramping, bloating, constipation or diarrhea after taking the contrast.

**CT Scan**

**Procedures:** You will have a CT (Computed Tomography) scan at months [X] and [Y]. The CT scanner is a doughnut-shaped machine that uses x-rays to create computer pictures showing the inside of your body. During the procedure, you will need to lie still on a table inside the CT machine. The table will move you in and out of the machine during the scan and you will be instructed to hold your breath. The scan itself will only take a few minutes to complete, the entire visit will take about 30 minutes.

**Risks:** See “Radiation” below & “Contrast Agent” above.
Discarded Tissue

Procedures: Normally during surgery small amounts of tissue are removed and discarded. At the end of your surgery, we will collect any tissue that has been removed instead of discarding it. Collecting this tissue for the purposes of this study will not affect the process or outcome of your surgery. No extra tissue will be removed for this study.

Discovery of Previously Unknown Condition(s)

Risks: As a result of the tests completed as part of this study, we may discover that you have a medical condition that you did not previously know about. If we discover something new as a result of these tests you will be told about it. The study doctor/staff will talk with you about the findings and your options. You may be told to follow up with your regular doctor or other specialists for future care.

Dose Escalation

Procedures: The dose of [X] you receive will depend on when you join the study. We will begin with a low dose. If subjects on one particular dose have no serious side effects, the next group of subjects will receive a higher dose. If you experience a serious side effect, the drug will be stopped. You’ll be asked to continue in the study for the remainder of the visits even if you stop taking the study drug. The study doctor will tell you what dose you will receive before you make a decision about taking part in this study.

DXA

Procedures: You will have a DXA (Dual energy X-Ray Absorptometry) scan to measure your bone density. This procedure will take place at [X] and will take about [20 minutes] to complete. During that time you will need to lie still on a padded table while the instrument scans your body. We will do [3] different scans: [1 of your whole body, 1 of your lower back, and 1 of your forearm].

Risks: See “Radiation Exposure” below.

Echocardiogram and/or Electrocardiogram

Procedures: Based upon your personal and family history, you may need to have an echocardiogram and/or electrocardiogram done. An echocardiogram is a painless test using sound waves that takes a 2-dimensional picture of your heart. You will need to lie still on a table for about 20 minutes while the test is being done. An electrocardiogram (ECG) is another painless test that is performed while you lie still for about 5 minutes. It involves placing electrodes on the chest and arms/legs and recording the electrical activity of your heart. If you have already had these tests as part of your regular medical care we may ask to get the results from your physician and you will not need to undergo any further testing.

Risks: Other than possibly experiencing some minor skin irritation from the electrodes there are no anticipated risks related to complete the electrocardiogram.

Also see “Discovery of Previously Unknown Condition” above.

e-Records

Procedures: The results from the laboratory and diagnostic tests conducted for this study will be placed in the [Strong Memorial Hospital] electronic medical record, along with documentation of all of your study visits.

Exercise Testing

Procedures: At study visit [X], you will complete an exercise test. This test involves walking and running on a treadmill while hooked up to a monitor to measure your heart rate and rhythm and blood pressure. You will also be asked to wear a mouth piece and a clip on your nose during the test so that we can take breathing measurements. To start, the treadmill will be set at slow walk speed but will be increased to slightly faster speeds and higher inclines every couple of minutes. You will be encouraged to give as much effort as you can and to keep going until you feel too
tired to continue. Once you reach that point, you can tell the study team and they will slow down the treadmill and decrease the incline. You will be asked to continue walking on the treadmill until you are comfortably walking. Your blood pressure, heart and breathing rates will continue to be monitored for an additional 15 minutes after you have completed the test.

**Risks:** The exercise test may cause muscle soreness, dizziness, shortness of breath, lightheadedness, chest pain or you may feel faint. There is also the possibility of tripping or falling while on the treadmill. You will be monitored throughout the test by the study doctor.

**Focus Group**

**Procedures:** You will be asked to take part in a focus group led by one of the investigators. The group will have about [10] members and will last for [about an hour]. During that time you and the other group members will be asked questions about your opinions and experiences with [X, Y and Z]. You will be asked to keep what is said during the group discussion between the subjects only.

**Risks:** See “Invasion of Privacy/Breach in Confidentiality” below.

**Genetic Testing (as defined by NYS law)**

**Procedures:** As part of this study, we will draw a small sample of blood [(about 2 tablespoons)]. Your blood sample will be sent to laboratory at [X] and DNA (genetic material) will be extracted from it to complete genetic testing and determine whether you are predisposed to developing [X]. Your DNA stores information in a code and serves as a blueprint for how the cells in your body work. The code carried in your genes is inherited from your parents and can tell things about a person’s risk for certain diseases and how they will respond to treatment. As part of this study, we will not only look to see if you are prone to developing [X], but also compare the results to information we find during your physical examination.

Before you decide to be in this study and undergo this test, you may wish to speak to a genetic counselor. Genetic counselors are medical professionals who advise people on the nature and potential consequences of genetic testing. You may also choose whether or not you wish to receive the results of this testing. If you decide to receive your results, the study team will notify you by phone and answer any questions you have. A positive test confirms the presence of a genetic mutation and, at present, puts individuals at a [Y]% chance of developing [X] (compared to the [Z]% chance that the general population has for developing [X]). If there is a positive test result, you may want to consider further independent testing, pursue genetic counseling or follow up with your regular doctor. If, for some reason, the results of your test are uncertain or out of the ordinary, you will be asked to provide an additional blood sample for repeat testing.

**Risks:** You will experience minor discomfort and rarely bruising, dizziness, fainting or infection as a result of the blood draw. Only the tests described in this consent form will be completed on your blood sample and the sample will be destroyed [at the end of the study].

The uncertainty of finding out whether or not you are predisposed to developing [X], as well as finding out the results of the testing, may make you feel anxious. Please contact us before or after the test, if you wish to speak to someone about this.

The results of the genetic testing may affect your employment and ability to obtain certain types of insurance. A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans and most employers to discriminate against you based on your genetic information. However, it does not protect you against discrimination by companies that sell life insurance, disability insurance or long-term care insurance.

There are also risks related to invasion of privacy and breach in confidentiality. We will remove your name and any other identifying information that could directly identify you from your study information and blood sample and replace it with a subject code. Only a few study team
members will have access to the database that will link your code with your identifying information. Other investigators and study team members will only have access to coded information. No study information, including the results of your genetic testing, will be disclosed outside of the individuals working on this study. If we decide to share the results of your testing with other people or groups not listed on this form, we will contact you to get your consent first.

**Written Assent:** We will collect a small blood sample from a vein in your arm to obtain a sample of your DNA. DNA is inherited from your parents and decides things like what color hair and eyes you have. It can also put you at risk for certain diseases. We will test the sample we collect to see if you have the gene for [X]. If your test is positive, the study doctor will talk to you and your parents about what this means and what other doctors you might need to see.

**Genomic Research (Genetic research that does not meet the definition of “genetic testing” as defined by NYS law)**

**Procedures:** We will collect a saliva (spit) sample from both you and your child by gently rubbing a swab inside your mouth. Saliva and other tissue in your body contain genes, which are made up of DNA. DNA acts as the body’s blueprint for how our bodies work including how we respond to disease. All of the saliva samples we collect will be coded with a number and sent to [X] to look at genes. We hope to find out if there is a genetic (inherited) cause for [X] or if genes affect the severity of [X].

**Risks:** There are no physical risks related to obtaining the saliva sample. You should be aware however, that because we are looking at both parent/child genes, the research may determine that the father of the child is someone other than who it is thought to be (non-paternity). Non-paternity will be kept confidential and will not be shared, even with you or your family members.

To protect your/your child’s privacy we have several safety measures in place. We will remove your/your child’s name and any other identifying information that could directly identify you from your saliva sample and replace it with a subject number. All other study information will be stored in a secure manner and only study personnel will have access to this information. However, because your genetic information is unique to you we cannot guarantee that your identity will never become known.

Some genetic information can help predict future health problems of you and your family and this information might be of interest to your employers or insurers. A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans and most employers to discriminate against you based on your genetic information. However, it does not protect you against discrimination by companies that sell life insurance, disability insurance or long-term care insurance.

**HIV Testing**

**Procedures:** You will be tested for HIV as part of the screening visit before you actually start the study. You will need to sign a separate consent form for this procedure. If you are found to be HIV positive you will not be able to participate in this study. You will also be offered counseling about HIV infection and notification of any partners. Per New York State law, your name will be released to the State Department of Health. Your medical records will be kept confidential to the extent permitted by law.

**Risks:** See “Blood Draws” above and “Invasion of Privacy/Breach in Confidentiality” below.

**IV (Intravenous Catheter)**

**Procedures:** You will receive either the study drug or placebo through an IV, which is a small plastic tube inserted into a vein in your arm using a needle. This may require that saline water be inserted into the tube to keep the tube from clogging.
**Risks:** The risks of IV insertion include temporary pain and bleeding or bruising at the site where the IV enters the skin. In placing the IV, there is a small chance of fluid leaking into the tissue surrounding the IV and infection, which would require treatment with antibiotics. Rarely, the IV may need to be removed and a second one inserted.

**Interview**  
*Procedures:* You will be interviewed for [about an hour] by a member of the study team in a private office. The study team member will ask you questions about your experiences with [X, Y and Z].

*Risks:* Some of the questions the interviewer will ask may be upsetting or make you feel uncomfortable. You do not have to answer any questions you do not want to answer and you can stop at any time.

Also See "Invasion of Privacy/Breach in Confidentiality" below.

**Invasion of Privacy/Breach in Confidentiality**  
*Risks:* Because this study involves collecting personal, identifiable information about you, there is a potential for invasion of privacy or breach in confidentiality. To minimize this risk, we will assign you a study number instead of labeling the information we collect from you with your name [or medical record number]. All of the information we collect will be stored in a secure manner and only study team members will have access to it.

**Lumbar Puncture**  
*Procedures:* You will undergo a lumbar puncture (sometimes called a “spinal tap”) to obtain cerebral spinal fluid (CSF) samples at visits [X and Y]. This procedure involves inserting a small needle into your lower back. The study staff will help position you either on your side or sitting up, whichever is most comfortable for you. The lower part of your back will first be cleaned with antiseptic and then the study doctor will inject a small amount of local anesthetic to numb the area. Once numb, a very thin needle will be inserted into the spinal canal in your lower back [well below where the spinal cord ends]. About [X] teaspoons of spinal fluid will be removed for analysis and storage. Your body usually replaces this fluid within 1-2 hours.

After the lumbar puncture is complete, you will remain in the clinic for about 30 minutes. To prevent side effects, it is important that you do not do any strenuous physical activity for 24 hours following the procedure. This includes lifting, bending, doing housework and gardening, or exercising.

*Risks:* The lumbar puncture may cause pain at the site where the needle goes in and the spinal fluid is taken. There is a small risk of infection or bleeding. After the lumbar puncture you may get a headache. To minimize the risk of a headache the doctor will use a small needle and may prescribe bed rest for one or more hours after the procedure. If a headache occurs, it is usually mild and can be controlled by bed rest, drinking lots of fluids and a pain pill, such as Tylenol. Rarely, the headache is severe and may require additional treatment with a “blood patch”. In this procedure, a small amount of blood is injected into the lumbar puncture site. This procedure is generally effective in stopping the headache. To minimize these risks, the lumbar puncture procedure will be performed by a medical professional specifically trained to do this procedure.

Also see “Allergic Reaction” above for risks related to the use of lidocaine.

**MRI**  
*Procedures:* At visit [X and Y] you will have an MRI (Magnetic Resonance Imaging) done at [Strong Memorial Hospital]. An MRI creates pictures of the inside of your body using strong magnets instead of x-ray energy. At the time of each scan you will be asked to fill out a screening form to verify that it is safe for you to have the scan. You will also be asked to remove any metallic objects you may be wearing (for example, watches, earrings or piercings) and possibly to
change into a hospital gown. Then you’ll be asked to lie on a narrow bed that will move into the MRI scanner. [Before moving you into the scanner, special padding will be placed around your head to help keep your head still.] Once you are comfortable, the table will be moved into the scanner (the scanner is a long, narrow tube that is open at each end). You will need to lie still on the table during the scan which will take about [30 minutes] to complete. You will hear normal “hammering” or clicking and squealing noises during the scan. You will be able to communicate with the technician running the scan the entire time and will be provided an emergency button to squeeze at any time if you decide you want the scan to stop.

**Risks:** The MRI procedure uses a powerful magnetic field to generate images of the body. The magnet could move objects within your body that contain metal such as implants, clips or pacemakers. Certain magnetic imaging devices, such as 3T MRI machines, can demagnetize cochlear implants. If you have any of these items you should not participate in this study.

MRI scanning is painless but you may feel uncomfortable or claustrophobic in the machine. Earplugs will be provided to protect your ears. Rarely, contact with conductive materials (like wires) in the machine can result in excessive heating or burns during the scan. If you feel any heating or burning or sensations during the scan, please let the technician know.

**Nasal Wash**

*Procedures:* We will do a nasal wash at study visits [X, Y and Z]. To do this, a small amount of salt water will be put into each side of your nose and then suctioned out.

**Risks:** The nasal wash may cause sneezing and minor irritation of the nose and throat.

**Oral Glucose Tolerance Test**

*Procedures:* An Oral Glucose Tolerance Test (OGTT) will be done during visits [X and Y] to measure the level of glucose and insulin in your blood. You will be given specific instructions for your diet for the day prior to testing. Test instructions will be specific to each individual subject. Generally the test will include the following procedures:

- After 10 pm the night before the test and on the morning of the test, you should only drink water – no other foods or liquids; this is called “fasting.”
- An intravenous (IV) needle and tube will be placed in your arm so that we can do multiple blood draws without having to “stick” you each time. The needle will stay in your arm for the entire length of the test.
- Then you will be asked to drink [X].
- Blood will be drawn about every ½ hour from the IV over the following 4 hours.

**Risks:** Fasting prior to the OGTT may make you feel light-headed or dizzy. You may also feel weak, hungry, nervous or restless towards the end of the test as your blood glucose levels may drop. The risks of IV insertion include temporary pain and bleeding or bruising at the site where the IV enters the skin. In placing the IV, there is a small chance of fluid leaking into the tissue surrounding the IV and infection, which would require treatment with antibiotics. Rarely, the IV may need to be removed and a second one inserted.

**PET Scan**

*Procedures:* You will have PET (Positron Emission Tomography) scan at visits [Y and Z]. The PET scanner is a doughnut-shaped machine that uses x-rays combined with a dose of a radioactive substance (tracer) to create computer pictures showing the inside of your body.

Before the scan, you will have a radioactive substance injected into your arm after which, you will need to wait for approximately 30 minutes for the substance to be absorbed. After 30 minutes, you’ll lie on a narrow, padded table and be positioned for the scan. The scan itself is painless and won’t make much noise. During this time you will need to lie very still. It will take about another 30 minutes to complete.
**Placebo**

*Procedures:* A placebo is a substance that looks like the study drug but doesn’t include any active ingredients.

**Pregnancy**

*Risks:* You cannot participate in this study if:
- You are pregnant;
- You or your partner are planning to become pregnant while in the study [(for the next 2 years)]; or
- You are breastfeeding.

Study procedures in this research project may have risks to your unborn or nursing child. If you are female, you will be given a pregnancy test before you start the study and at each study visit during the course of the study.

If you join this study, you and your partner must agree to use birth control during the study [(for the next 2 years)]. The study team will talk about different methods of birth control with you. Both men and women in this study must agree to use birth control.

If you or your partner should become pregnant while in this study, or if you think that you or your partner has become pregnant, you must contact the study team right away. If you or your partner becomes pregnant, you will have to stop taking the study drug and the study staff will ask to follow the pregnancy to term.

*Written Assent:* The study drug may hurt an unborn child. If you are sexually active, the study doctor will talk with you about using birth control while participating in this study. If you or your partner becomes pregnant while you’re in the study, you must tell the study doctor immediately. If you are female, you will have a urine pregnancy test completed at each of the study visits.

**Questionnaires**

*Procedures:* We will ask you to complete [3] questionnaires that will take approximately [10 minutes] to complete. The questionnaires will ask you about [the symptoms you’re experiencing, your ability to complete everyday activities and will test your memory and concentration.]

*Risks:* Some of the questions in the questionnaire may be upsetting or make you feel uncomfortable. You can skip any of the questions you do not want to answer and you can stop at any time.

Also See “Invasion of Privacy/Breach in Confidentiality” below.

**Radiation**

*Risks:* Participation in this research involves exposure to radiation from [x-rays, the CT scans, the DXA scan, etc.]. You are exposed to radiation on a daily basis from both natural (sun and earth) and manmade sources. The estimated amount of radiation exposure that you will receive from this procedure is about [X]. This is about [Y]% of what you would normally be exposed to over the course of a year. There is no expected risk form the amount of radiation you will be exposed to for the purposes of this study but you should understand that the risks associated with radiation exposure depend on your repeated exposure over time. There is no known minimum level of radiation exposure that is recognized as being totally free of the risk. The more radiation you are exposed to over time, the greater the risk. You should inform the study team of any other x-ray exposure you may be receiving during your participation in this study.

**Randomization**
**Procedures:** If you decide to participate in this study, you will be assigned by chance (like flipping a coin) to one of two groups. Group 1 will receive [X] and Group 2 will receive [Y]. There is an equal chance that you will be assigned to either group. [Neither you nor your doctor will be able to know to which group you are assigned].

You will be randomized into one of three study groups. Randomization means that you are assigned by chance (like pulling a number from a hat) into one of the groups described below:
- If you are in Group 1, you will…
- If you are in Group 2, you will…
- If you are in Group 3, you will…

**Study Drug**

**Procedures:** You will be instructed to take [1 tablet] of the study drug [twice a day (once in the morning and once in the evening)] for [4 months]. [The study drug should be taken with food and a full glass of water (at least 1 cup).] [To help you remember to take the drug and to report any side effects, you will be provided a diary to complete each day while you participate. You will be asked to bring the study drug and diary with you to each of your study visits.]

**Risks:** The study team will monitor you carefully for any side effects of the study drug. Side effects may include…[depending on the side effects it may be helpful to provide a list or table and categorize as Likely, Less Likely and Rarely (Rarely being ≤1% of cases)].

During the study, if you are having problems with the study drug or are experiencing side effects you should tell us so that we can determine if it is necessary for you to reduce the dose or stop taking the drug. If you experience significant side effects, please contact us immediately. If you stop taking the medication, we would still like you to continue to participate in other parts of the study, for example, [X and Y].

**Tissue Banking**

**Procedures:** We would like to keep any left over tissue samples from [the extra biopsy that is being completed as part of this study and from your surgery] for future research. Normally this tissue is thrown away but, with your permission, we will “bank” (store) the tissue. No extra tissue will be removed during the biopsy or surgery.

The tissue that is banked will only be used for research to learn more about [X]. Future research may include looking at differences in certain genes (DNA), for example, to see how they may predict responses to a certain drug. For certain types of future testing we may need to contact you to obtain your consent before completing the testing.

All banked tissue will be stored indefinitely at [Y]. Your tissue that is sent there will have all of your personally identifying information removed and will be labeled with a code. Only study team members at the University of Rochester will have the information that matches the code to you. Other researchers that my use your tissue for research will not have access to this information. In the event that other researchers using your tissue want to know more about your health we will contact you and you can decide at that time whether or not you want any other information shared.

The decision to let us keep the left over tissue is up to you. Allowing us to contact you in the future is also optional. You can still be a part of the study even if you say “no” to banking the left over tissue. No matter what decision you make, it will not affect your care. If you decide now that your tissue can be used for future research, you can change your mind at any time. If you do change your mind, please contact [insert name of contact person] at [insert contact information]. Any identified tissue that remains at that time will then be discarded (samples that have been already used, or any data that has been generated as a result of testing done on your sample will not be able to be retrieved or destroyed). You will be asked to indicate your preferences regarding tissue banking and future contact at the end of this consent form.
**Risks:** We do not anticipate any risks to banking your tissue other than the potential loss of privacy. As described above, we will code your tissue to help protect you. Because the genetic information in your tissue is unique to you, it may be possible that someday in the future your tissue could be linked back to you just based on your genes (even though directly identifying information will not be stored with the tissue).

**Prior to Signature Blocks:** Please mark an X in the boxes below to indicate if you want to donate your left over tissue for future research.

- [ ] Yes, I want my left over tissue stored for future research. Please also check one of the following:
  - [ ] Yes, I agree to be contacted in the future about my stored tissue.
  - [ ] No, I do not want to be contacted in the future about my stored tissue.
- [ ] No, I do not want my left over tissue to be stored for future research.

**Written Assent:** We would like to keep any left over tissue samples for use in future research. All left over tissue will be stored in a way that will protect your privacy (we will use a number instead of your name to label samples). Allowing us to keep this tissue is up to you. You can still be in the study and decide that you don’t want us to keep the left over tissue. You can also say “yes” now and change your mind later. If you change your mind later, you can contact [insert name of contact person] at [insert contact information] to have your left over tissue destroyed. At the end of this form, you’ll be able to tell us whether or not keep the left over tissue for research. [Provide checkboxes at the end of the form as appropriate.]

**Washout Periods/Withdrawing Current Medication Procedures:** The medication you normally take for your condition will need to be stopped about [X days] before you can start taking the study drug. You will not be able to start taking the medication again until after you’ve completed or withdrawn from the study. [Based on your randomization assignment, you may receive no active medication (placebo) or] the study drug may not be a dose that will help your condition. As a result, you may experience an increase in symptoms including [X, Y and Z]. If your symptoms worsen or make you comfortable, talk to the study doctor about withdrawing from the study.

**X-Ray Procedures:** As part of your regular care you will have x-rays of your hip taken at [A days, B weeks and C, D and E months] after your surgery. For the purposes of this study, we will ask you to have additional x-rays done at [X and Y].

**Risks:** See “Radiation” above.
APPENDIX 2 : Frequently Asked Questions

1. I just downloaded my watermarked consent documents and the formatting doesn't look right. What should I do?

First, check the original document that is uploaded in the RSRB application. If the formatting on this document is off, the only way to correct it is by submitting a revised document via amendment in ROSS. If the original document is correct and it appears that inserting the watermark changed the formatting, please contact our Data Manager at 275-3050.

2. We would like to mail consents to subjects to review, sign and return. Is this allowed? What would be the best procedure for implementing this?

Yes, obtaining written consent via mail is allowed assuming that it is appropriate for the study and there is sufficient oral/in-person contact regarding the study prior to mailing the document (for example if the consent discussion is conducted over the telephone). If you will be obtaining consent via mail consistently, your process should be described in the study protocol. On the other hand, if you plan to obtain written consent in person and a situation arises where obtaining consent via mail is necessary, it would be best to confirm with your IRB specialist that obtaining consent via mail is appropriate and then document the process in the subject’s study file. In cases where subjects are being re-consented via mail (e.g., when study procedures have changed and re-consent is required), your process for re-consenting via mail should be described in the amendment making the changes to the consent document.

The process for obtaining consent via mail can be accomplished in 1 of 2 ways:

- Mail 2 consents forms to the subject. Instruct the subject to sign both, keep one for their records and mail back the second; or
- Mail 1 consent form to the subject. Instruct them to sign the document and mail it back to the study. Upon receipt of the consent, the person obtaining consent would then sign the document and mail a copy of the entire document (with both signatures) back to the subject.

Regardless of which procedure is followed, a letter should accompany the consent form in the mail providing subjects instructions for completing the form as well as providing contact information if additional questions arise (self-addressed stamped envelopes should also be included).

3. Would the use of an “opt out” consent be permissible?

No, the RSRB does not permit the use of “opt out” consents. All subjects should be provided the opportunity to actively consent for participation in a study and additional efforts should not
be required on the part of a subject who does not want to participate in the study (e.g., asking subjects who do not want to participate to return a postcard/phone call to the study team indicating so).

4. **Who is allowed to obtain consent?**

While the federal regulations do not specify who should (or is allowed to) obtain consent, they do give the ultimate responsibility to the principal investigator, who may delegate to appropriately trained personnel. The RSRB requires that any investigator or other study personnel who may obtain consent complete the appropriate HSPP/EPRP training (based on the risk level of the study) and be listed on the RSRB application.

The training/background of the study team member(s) responsible for obtaining consent should be appropriate based on the nature and design of the study. For studies involving the use of an investigational drug or device, it may be necessary to involve a nurse or physician team member in order to ensure that questions are answered appropriately. If a study is particularly complex it may not be appropriate for a student team member to obtain consent.

In some cases a protocol or standard operating procedure may further delineate who can/cannot obtain consent (e.g., an industry-initiated study protocol that specifies that only the principal investigator obtain consent). Any additional conditions provided in a study protocol or standard operating procedure must also be adhered to in addition to RSRB requirements.

5. **The signature block for the person obtaining consent states “I have given the subject adequate opportunity to read the consent before signing.” What is considered “adequate opportunity” for the subject to read the consent and consider participation before signing the consent form?**

While there are no specific guidelines on how much time should be given to potential subjects to consider participation, it is good practice to estimate how much time a “reasonable person” would need to do so. The amount of time one might need to consider participation depends on multiple factors: the complexity of the study design & procedures, the study population, the setting in which the subject is approached for participation, and the readability of the consent document. For example, it may take a couple of meetings for a potential subject to not only understand the cancer they may have just been diagnosed with but also to understand the study as well as other treatment options.

The bottom line is, there should sufficient time for a “reasonable person” to read the form, ask questions and receive answers and consider their participation (potentially with the help of other friends/family). Generally speaking, unless it is a life-threatening situation, potential subjects should not feel rushed and should be given as much time as possible to consider their participation.

6. **Do we need to keep a copy of the signed consent form in the medical record?**

Clinical investigators may wish to place copies of the research consent forms in the medical record to inform/alert health care providers. While this is not necessarily required for all studies, it may be an important consideration in drug/device studies where it is vital for clinical providers to be aware of a subject’s participation in a study.

For consent documents that are to be retained in the subject’s medical record, use the Strong Memorial/Highland Hospital form number SMH-101 or HH-101, respectively, in the upper right-hand corner and provide space either for addressograph or hand entry of the subject’s name and chart number. (Note: the original signed consent form should be kept by the investigator in the study records; only copies should be placed in the medical record.)
APPENDIX 3 : Additional Resources

DHHS, OHRP & FDA:

- OHRP Informed Consent FAQs: http://answers.hhs.gov/ohrp/categories/1566
- OHRP Video – General IC Requirements: http://www.youtube.com/watch?v=URo4x4pv68A&p=5965CB14C2506914

Plain Language Thesauruses & Health Literacy Tools:

- URMC Miner Library - Health Literacy Toolkit: http://www.urmc.rochester.edu/hslt/miner/selected_topics/HealthLiteracyToolkit.cfm

Books: